

## Follow-up Care in Childhood Cancer Survivors: Improving Services in Switzerland

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### Introduction

The survival rate of children and adolescents diagnosed with cancer has markedly improved in the last decades and now exceeds 85% in Switzerland [1]. This results in about 5700 childhood cancer survivors living in Switzerland, who have been diagnosed before age 14 years [2]. Most childhood cancer patients are cured from cancer and have decades of life ahead of them. Therefore, effective strategies to promote long-term health and quality of life are important. In this paper, we will briefly present major late effects experienced by childhood cancer survivors, and describe ongoing initiatives in the field of childhood cancer survivorship and long-term follow-up care (LTFU) in Switzerland.

### Late Effects

#### *Medical late effects*

Long-term complications and disabilities resulting from treatment toxicity or from the cancer itself can lead to chronic ill health and increased mortality years and decades after cancer diagnosis [3, 4]. A large proportion of childhood cancer survivors experience late effects. At 45

years of age 95% have at least one chronic health condition and 80% have a severe, life-threatening, or disabling condition [5]. Frequently reported late effects are second primary cancers, cardiovascular diseases, endocrine disorders, musculoskeletal problems, and secondary malignancies [3]. In Switzerland, we found that survivors had a 2-14 times higher risk to develop cardiovascular diseases [6], hearing loss [7], or pulmonary diseases [8] than their siblings. As the first generation of survivors' age into their 50s and 60s, it becomes evident that these chronic health conditions occur earlier than in peers and increase substantially over time.

#### *Psychosocial late effects*

Late effects of childhood cancer are not limited to physical health, they include social and psychological problems, such as academic and employment difficulties, financial and insurance problems, psychological distress, and difficulties with family and intimate relationships [9]. Although many survivors adapt well and experience positive psychological changes such as posttraumatic growth [10], around 1 in 4 is at risk for psychosocial sequelae [9, 11]. The risk for psychological distress and related psychosocial needs is particularly high in women, those with a migration background, those with low household incomes, without siblings, who are older than 25 years of age, with cancer diagnosis between 5-14 years of age, and those with late effects [9, 12]. Most survivors report having at least one unmet psychosocial need [13], and different needs arise at different times of the cancer-survivorship trajectory. Unmet needs include tailored age-specific personalized information on late effects, lack of organized LTFU care, and support for psychological distress [14].

## Research initiatives in childhood cancer survivorship: The current landscape in Switzerland

The Swiss Childhood Cancer Survivor Study (SCCSS) is a population-based, long-term cohort study [15] of all childhood cancer patients registered in the Swiss Childhood Cancer Registry ([www.childhoodcancerregistry.ch](http://www.childhoodcancerregistry.ch)) [16] since 1976. It monitors long-term outcomes and investigates factors associated with prognosis. It does not only assess survival on a national level, but also somatic health, chronic diseases, health behaviors, psychological and social wellbeing, and quality of life. Currently, it includes information on survival and second primary cancers from over 7600 survivors, and patient-reported outcomes data from over 3100 survivors and over 900 siblings [2]. The SCCSS analyses information from various sources: routine data on mortality and hospitalizations from the Swiss Federal Statistical office, incidence of secondary cancers from the cantonal cancer registries; patient-reported data from questionnaires; and detailed data on chemotherapy and radiotherapy, and on health outcomes from hospital charts. In addition to questionnaire-based research, the SCCSS recently has started to collect clinical data from standardized follow-up examinations in Swiss Pediatric Oncology clinics. This allows to identify late effects at an early stage, for instance by echocardiography, audiometry or lung function tests, and thus to optimize and individualize follow-up care and secondary prevention. The SCCSS collaborates closely with survivors, their parents and physicians, so that results are immediately available to inform health care and supportive services.

The Pediatric Oncology-Hematology clinic in Geneva (Prof. Marc Ansari) hosts the national Germline DNA Biobank Switzerland for Childhood Cancer and Blood Disorders (BISKIDS). There, germline DNA is collected on a national level from all childhood cancer patients and survivors. Analysis of gene-treatment interactions will enable researchers to develop more personalized therapy and care in the future. The Children's Hospital Zurich (Prof. Jean-Pierre Bourquin) leads the National Swiss Pediatric Hematology/Oncology Biobanking Network (SPHO), a collection of liquid and solid tumour tissue samples. Both biobanks closely collaborate with the SCCSS. A national IT platform to link these three datasets is currently being developed in the framework of an SNF Biolink grant (The Swiss Pediatric Hematology/Oncology Metabank – a network for precision medicine research). This national platform will contain a comprehensive dataset for future patient-centred high-quality research.

The University of Luzern has a focus on psychosocial aspects of childhood cancer and survivorship covering psychosocial problems in survivors and the family. Their research additionally addresses the organisation of LTFU, especially psychosocial LTFU.

Finally, researchers from the University of Bern and Luzern collaborate in the International Guideline Harmonization Group (IGHG, <http://www.ighg.org/>), where they write systematic reviews and develop evidence-based, standardized guidelines for clinical follow-up to improve the health and quality of life of childhood cancer survivors in Switzerland and worldwide.

## Swiss services for childhood cancer survivors

The national organization Childhood Cancer Switzerland supports initiatives to improve follow-up care and collaborates closely with the international childhood cancer community. They recently established the Competence Center for Survivorship Issues, which offers a unique possibility for survivors and health care professionals to get support and information about LTFU and planned activities to meet, support, and exchange experiences. It organizes conferences, workshops and campaigns to raise the awareness of late effects and LTFU. Their active involvement in the pediatric Swiss LTFU working group, consisting of health care professionals, researchers, survivors, and parent representatives, reassures survivors input in LTFU initiatives. The LTFU working group aims to improve LTFU strategies through extensive exchange and collaboration between the different stakeholders and the SPOG clinics. Recently, the working group endorsed the use of similar evidence-based late effect guidelines as a basis for the personalized LTFU recommendations in a position statement paper [17].

## Long term follow-up

With the growing population of childhood cancer survivors, there is an increasing need to develop a range of support services of LTFU care in Switzerland that addresses medical and psychosocial issues. A systematic transition into adult care is necessary to avoid the risk of losing survivors to LTFU. Currently, all Swiss pediatric oncology clinics offer follow up care for at least 5-10 years [18]. However, only around 1 in every 4 survivors aged more than 20 years attends LTFU after their discharge from Pediatric Oncology [19]. To improve the transition of LTFU in the adult care setting [17], it is important to establish multidisciplinary teams, which include adult specialists who work closely with pediatric oncologists and incorporate psychosocial support and vocational/academic counseling. Recently, more attention is being given to LTFU in Switzerland, which led to the first interdisciplinary LTFU clinics for adult childhood cancer survivors in Aarau, Bern, Geneva, and Liestal. More information about these LTFU clinics can be found on the website of Childhood Cancer Switzerland (<https://www.kinderkrebs-schweiz.ch>). The majority of these LTFU clinics use comprehensive treatment summaries or survivor care plans at the time

of transition into adult care, with individualized LTFU recommendations based on earlier treatment. North-American initiatives for personalized recommendations are implemented in Bern, Liestal (Passport for Care®), and Aarau (St. Jude's survivorship care plan). These treatment summaries and care plans give survivors the necessary information to take responsibility of their own health. Furthermore, the increased awareness through survivorship networks results in higher LTFU care demands, particularly among older survivors who were previously lost to follow-up. This highlights the importance of harmonizing LTFU procedures within Switzerland and the need for reimbursement. There is also a need to raise awareness of interdisciplinary care of childhood cancer survivors among family doctors and specialists.

In summary, the close collaboration between pediatric oncology and patient representatives has allowed to set up a large national network for comprehensive survivorship research, which encompasses assessment of patient reported outcomes, monitoring of early late effects, establishment of germline DNA and tumor biobanks, and comprehensive psychosocial and healthcare research on a national level. In the next years, priority should be given to raise awareness among health care professionals and survivors and to harmonize LTFU care services and survivorship care plans.

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